REMARKS

Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 20-22 and 43-47 stand rejected for allegedly lacking enablement. The Examiner alleges that a full teaching and exemplification of the claimed invention is required for enablement because the nature of the invention is complex, and that the complex nature of the claimed subject matter is exacerbated by the breath of the claims. Specifically, the Examiner contends that the application fails to teach which one of the nitric oxide inhibitors would be effective, and the dosage of the inhibitor. Applicants traverse.

Claims 20-22 and 43-47 are directed to a method of increasing a population of dividing cells in a tissue of a mammal using a nitric oxide inhibitor. These claims are based on applicants' discovery that the inhibition of nitric oxide function promotes cell proliferation. This is not a tissue-specific event.

Applicants disclose a number of nitric oxide inhibitors including nitric oxide scavengers such as 2-phenyl 4,4,5,5-tetraethylimidazoline-l-oxyl-3-oxide (PTIO), 2-(4-carboxyphenyl)-4,4,5,5-tetraethylimidazoline-l-oxyl-3-oxide (Carboxy-PTIO) and N-methyl-D-glucamine dithiocarbamate (MGD); and nitric oxide synthase inhibitors such as N-nitro-L-arginine methyl-ester (L-NAME), N-monbmethyl-L-arginine (L-NMMA), 2-ethyl-2-thiopseudourea (ETU,), 2-methylisothiourea (SMT), 7-nitroindazole, aminoguanidine hemisulfate and diphenyleneiodonium (DPI) (see page 9, lines 9-15). All nitric oxide inhibitors are able to promote cell proliferation due to their ability to block the action of nitric oxide. Applicants' invention is premised on the discovery of this shared characteristic of nitric oxide inhibitors. This feature is common to all nitric oxide inhibitors and is not tissue specific.

The Examiner asserts that there is no guidance as to how much nitric oxide inhibitor to use to increase the population of dividing cells. Applicants disagree. The application teaches that the amount of nitric oxide inhibitor will depend on factors such as the nature of the condition and route of administration, and can be determined by standard clinical

techniques (see page 22, line 17 to page 23, line 2). Determining dosage does not constitute undue experimentation because it can be assessed using conventional methods well-known to the skilled artisan. There is **no** requirement under patent law to specify dosage in a claim when such information can be obtained by one skilled in the art without undue experimentation (MPEP 2164.01(c)).

The Examiner states that the guidance provided in the specification relates to increasing hematopoietic and bone cells, and that all of the working examples are directed to BrdU-labeled cells and hematopoiesis. The Examiner asserts that there is no nexus between the exemplified disclosure and the ability of nitric oxide inhibitors to increase a population of dividing cells as claimed by applicants. The Examiner further contends that the amount of experimentation required to practice the claimed invention is undue because of the lack of guidance. Applicants disagree.

The Examiner is mistaken in asserting that all of the working examples relate to hematopoiesis. In fact, the application exemplifies the successful use of nitric oxide inhibitors to increase the number of cells in animals as evolutionarily distant as insects, amphibians, and mammals, and in tissues as diverse as imaginal discs, brain, and hematopoietic tissue. (Example 1, page 23, line 7 to page 32, line 17; Example 2 at page 32, line 18 to page 39, line 6; Example 3, page 39, line 7 to page 43, line 11; and Example 4, page 43, line 12 to page52, line 2). In addition, BrdU is merely a marker to label dividing cells. BrdU does not reflect a specific tissue type and is not organism-specific.

Notwithstanding the successful use of nitric oxide inhibitors in various tissues of evolutionarily different animals described in the working examples, it is improper to limit applicants to what is exemplified in the application (MPEP 2164.02).The application discloses use of nitric oxide inhibitors to increase the number of cells in tissues other than hematopoietic tissue, including blood, skin, bone, digestive epithelium, neural tissue, muscle, cartilage, fat or adipose tissue, bone marrow stroma, tendon, brain, liver, reproductive organs, and pancreas

(see page 8, lines 18-20; and page 20, line 23 to page 21, line 28). As explained above, the ability to promote cell proliferation is due to the ability of nitric oxide inhibitors to block nitric oxide function. This characteristic of nitric oxide inhibitors is not tissue-specific. Furthermore, recent publications confirm applicants' invention. See , e.g., Packer et al., "Nitric Oxide negatively regulates mammalian adult neurogenesis," (2003) PNAS 100:9566-9571 (Packer; copy enclosed), which reports use of the nitric oxide inhibitor, L-NAME, to promote proliferation of neuronal cells in rat brain. Thus, there is ample disclosure in the application to guide the skilled artisan to practice the claimed invention without undue experimentation

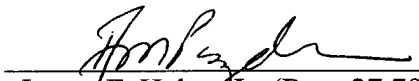
Accordingly, applicants respectfully submit that claims 20-22 and 43-47 are enabled.

CONCLUSION

In light of the foregoing amendments and remarks, applicants request that the Examiner withdraw all outstanding rejections and grant allowance of the pending claims.

The Examiner is invited to telephone applicants' representatives regarding any matter that may be handled by telephone to expedite allowance of the pending claims.

Respectfully submitted,



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